Remarks

Applicants gratefully acknowledges the Office's withdrawal of its rejections of claims 12, 15-18, 19-27 and 39 under 35 U.S.C. § 112, first paragraph, claims 12, 15, 16-18 under 35 U.S.C. § 112, second paragraph, claims 12 and 15-16 under 35 U.S.C. § 102(a), and claims 19 and 20 under 35 U.S.C. § 103(a).

REJECTION UNDER 35 U.S.C. § 101

Claims 12, 25, and 39 stand rejected under 35 U.S.C. § 101 for allegedly encompassing non-statutory subject matter, i.e. a product of nature. Claims 12 and 25 have been amended as suggested to recite "an isolated polynucleotide" of artemin, which does not naturally occur in this form. Applicants, therefore, submit that amendments to claims 12 and 25 obviate the Office's rejection of claims 12, 25, and 39, and respectfully request that the rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 12, 15-26, 39-40 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. First, the Office contends that there is no adequate guidance in the specification for the recitation of "fragments" in claims 12, 15, and 25. Second, the Office alleges that the language "at least 65% identical" in claims 12, 15, 25, and 27 is overly broad. Third, the Office alleges that the specification fails to provide adequate guidance on which of the nucleic acid sequences encompassed by the claim can be made and used to promote survival of neurons. Further, the Office states that the relationship between the structure of the polynucleotide encoding amino acid sequence is not correlated to the function of the encoded amino acid sequence.

With respect to "fragments," claims 12, 15, and 25 have been amended to recite a fragment "that is biologically equivalent to artemin". Support for the amended claims can be found in the specification, for example, on page 15, lines 27-30 and page 21, lines 16-26. Specifically, the amended claims comprise fragments that retain biological activity of artemin (that is, only fragments that promote survival of neurons).

A skilled artisan can, without undue experimentation, determine which fragments can promote survival of neurons. According to *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (P.T.O. Bd. of App. 1982), the test for enablement "is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a

reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed." The polypeptide sequence of artemin is relatively short, a mere 220 amino acids in length. Standard molecular biology techniques could be employed to produce polypeptide fragments of various sizes. The resulting polypeptide fragments can be readily tested for its ability to promote survival in neurons, as taught in Example 4, page 54-55 and Example 6, page 57.

With respect to the language "is at least 65% identical", the claims have been amended to recite "is at least 88% identical". Support for the amended claims can be found in the specification on page 18, where it shows that the sequence identity between human and mouse artemin is about 88%.

With respect to the Office's contention that the specification fails to provide adequate guidance as to which of the nucleic acid sequences encompassed by the claim can be made and used to promote survival of neurons, Applicants reassert the arguments stated above for "fragments". Specifically, a skilled artisan can, without undue experimentation, determine which polypeptides that meet the structural limitations of the claims also are biologically equivalent to artemin, i.e., will promote survival of neurons, thus meeting the functional limitation of the claims, and then routinely determine the nucleic acid sequences that encode those particular polypeptides. Thus, the claimed polynucleotides are adequately described, such that a skilled artisan would be able to make and use the invention.

The Office further states that the relationship between the structure of the polynucleotide encoding amino acid sequence is not correlated to the function of the encoded amino acid sequence. The claims have been amended to clarify that the function relates to the amino acid sequence and not the polynucleotide sequence.

For the above reasons, Applicants submit that the Office's rejection under 35 U.S.C. § 112, first paragraph, has been obviated, and therefore, respectfully request that the rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 12, 15, and 25 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Specifically, the Office alleges that the term "fragments" is vague.

Claims 12, 15, and 25 have been amended to recite fragments that have biological activity equivalent to artemin. Thus, only fragments with biological activities equivalent to artemin are within the scope of the claims. Moreover, the specification defines "biological equivalent" on page 15, lines 27-30. An example of a fragment that has biological activity equivalent to artemin is also provided on p. 21, lines 23-26.

A skilled artisan need not engage in any undue experimentation to practice the claimed invention. Using routine molecular biology techniques, he can produce artemin polypeptide fragments of various sizes. He can then readily test these artemin fragments for their ability to promote survival in neurons, using, for example, Example 4, pages 54-55 and Example 6, page 57. While some experimentation is required here, it is not undue because the methods are either routine and well within the ability of the skilled artisan, or alternatively are described fully in the specification (for example the cell survival assay described in Example 4). Further, given the relatively small size of the artemin polypeptide, the number of possible fragments thereof is small, and so even the quantity of experimentation required is limited.

Applicants submit that the amended claims are not indefinite, and respectfully request that the Office withdraw its rejection.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that each ground for the Office's rejections has been overcome or obviated, and that all the pending claims are in condition for allowance. Applicants respectfully request that such allowance be granted.

Respectfully submitted,

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AMENDED CLAIMS

12. (Four times amended) An isolated polynucleotide encoding a pan-growth factor which polynucleotide comprises a nucleotide sequence encoding a naturally occurring artemin amino acid sequence or a fragment thereof that is biologically equivalent to artemin and has at least 8 contiguous amino acids, wherein said nucleotide sequence comprises not more than 10,000 nucleotides, and wherein said artemin amino acid sequence is at least 88% identical to SEQ ID NO:26, and wherein said amino acid sequence promotes survival of neurons, and wherein said polynucleotide also comprises a nucleotide sequence encoding a polypeptide containing an active domain of at least one other growth factor from the TGF-β superfamily.

15. (Four times amended) An isolated nucleic acid molecule comprising no more than 10,000 nucleotides, wherein said nucleic acid molecule encodes a naturally occurring artemin amino acid sequence or a fragment thereof that is biologically equivalent to artemin, and wherein said artemin amino acid sequence is at least 88% identical to SEQ ID NO:26, and wherein said artemin amino acid promotes survival of neurons.

25. (Thrice amended) An isolated nucleic acid molecule comprising an artemin nucleotide sequence, wherein the artemin nucleotide sequence encodes a naturally occurring artemin amino acid sequence selected from the group consisting of a pre-pro-artemin polypeptide, a pro-artemin polypeptide, a mature artemin polypeptide and a fragment of said pre-pro-artemin amino acid sequence that is biologically equivalent to artemin and has at least 8 contiguous amino acids, and wherein the artemin amino acid sequence is at least 88% identical to SEQ ID NO:26 and wherein said amino acid sequence promotes survival of neurons.

27. (Thrice amended) An isolated nucleic acid molecule comprising a polynucleotide encoding:

(a) a pre- region of artemin as set forth in SEQ ID NO:54 or SEQ ID NO:55;

(b) a pro- region of artemin as set forth in SEQ ID NO:56 or SEQ ID NO:57;

(c) a pre-pro- region of artemin as set forth in SEQ ID NO:58 or SEQ ID NO:59; or

(d) a polypeptide that is at least 88% identical to (a), (b) or (c).